AF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Jerry M. COLLINS et al	Art Unit: 1616
Confirmation No.: 6698	Examiner: Dameron JONES
Appl. No: 10/088,561	
Filed: March 19, 2002	Atty. Docket No: 31978-178825
a. **For: IMAGING OF DRUG ACCUMULATION AS A GUIDE TO ANTITUMOR THERAPY**	Customer No: 26694 PATENT TRADEMARK OFFICE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to U.S. Patent and Trademark Office Official Gazette Notice dated July 12, 2005 ("OG Notice"), Applicants respectfully request pre-appeal brief review of the final rejection of claims 8-12 asserted in the final Office Action mailed March 30, 2005 ("final Office Action"), in the above-captioned application. This request is being filed concurrently with a Notice of Appeal. No amendments are being filed at this time.

The final Office Action rejects claims 8-12 under 35 U.S.C. § 112, second paragraph as failing to particularly point out and distinctly claim the invention. In particular, the rejection asserts that it is unclear what modulators are referred to in the phrase "modulators of cellular accumulation mechanisms" and "modulator" in claim 8. (See Office Action dated August 6, 2005.) The final

Office Action also states that the specification "does not set forth a group, class, compounds or clear definition of what species are encompassed by the phases [sic] that are compatible with the instant invention." (final Office Action pages 2-3.) The final Office Action also states that "the invention has not been described with such clarity that the reader is assured that the inventor actually has possession and knowledge of the modulators unique to the instant invention." (final Office Action page 3.) Applicants submit that this rejection is clearly not proper and lacks a clear legal basis. Accordingly, this rejection is ripe for the pre-appeal brief review process.

As set forth in MPEP § 2173.02, "In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent." (emphasis added) It is instructive that definiteness is to be measured "in light of

> (A) The content of the particular application disclosure;
> (B) The teachings of the prior art; and
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

MPEP 2173.02. No prior art has been cited with respect to the rejected claims. Therefore, what must be considered is the claim as a whole, the content of the application disclosure and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. As set forth more fully below, the present application includes description and claims directed toward uses of radio-labeled insoluble taxanes to measure drug accumulation in tumors. One of the described and claimed uses is for "monitoring changes in [drug] accumulation when a modulator is added [to determine] effectiveness of then modulator." (Specification, page 16, lines 13-14.) This use of the radio-labeled drugs does not require a specific compound as a modulator. Applicants submit that the application sufficiently defines the claims to persons of ordinary skill in the art, and that such persons would recognize what is clearly claimed in claims 8-12.

The final Office Action infers that, in order to be clear, the claims must set forth specific modulators. Reading the claim as a whole, this is simply not the case. Claims 8-12 (and 50-56) are directed to a method for "measuring the effectiveness of modulators of cellular accumulation" that requires, as one of the recited steps, "administering a modulator to a patient." (See Claim 8.) The claim does not require and is not limited to administration of a *specific* modulator. As set forth in the specification, there are a number of modulators known in the art. The present invention can be applied to measuring effectiveness of *any* modulator by "administering [an insoluble taxane] labeled with a positron-emitter to a patient; . . . and imaging at least part of the patient by PET to measure accumulation of the" insoluble taxane, as set forth in the application. (See Claim 8.) Properties of the modulator are not being measured, only the effect of the modulator on drug accumulation. Thus identifying the group, class, or compounds is not necessary. Furthermore, the inventors have invented a way to evaluate modulators. The claims are directed toward evaluation of any modulator and thus directed to modulators as a group, not a specific modulator. For at least this reason, the rejection is without basis.

All that is thus required to set forth the invention with particularity is what the steps are needed to measure the effectiveness of the modulator, and for persons of ordinary skill in the art to understand the term modulator as used in the claims. Applicants submit that the final Office Action does not assert that there is any ambiguity in the way in which the method steps are set forth. The issue then, is whether "modulators" is set forth clearly.

The previous response dated December 6, 2004, sets forth in detail how the modulators are identified, as a class, in the specification and included an excerpt from "The Encyclopedia of Cancer" describing one such modulator, in that case an efflux pump. Applicants submit that these cited portions clearly define modulators and efflux and influx pumps to a person of ordinary skill in the art. Those arguments are of record, are incorporated into this response by reference, and will not be repeated here.

The specification also teaches specific transporters and modulators, thus adequately defining by example what is meant by a modulator. Among the types of modulators mentioned in the specification are those affecting efflux pumps (or transporters), and influx pumps (or transporters),

cellular mechanisms that which move drugs and other compounds out of or into the cell, respectively. (See specification, page 15, line 28-page 16, line 4; page 16, lines 11-16.) Specific transporters identified in the specification include ATP-binding cassette (ABC) transporters, including MDR, MRP, and others. (See specification, page 15, lines 4-7.) Specific modulators identified in the specification include dexverapamil, PSC833, LY335979, GG918, VX-853 and Cremophor® (which is used in the intravenous formulation of Taxol®). (See specification, page 16, lines 19-22.) As set forth in the disclosure, "[t]he present invention may be utilized to monitor the effectiveness of these and other cellular accumulation modulators, such as the modulation of efflux mechanisms by any modulator including use of excipients used in formulations of drugs." (Specification, page 16, lines 23-26.) Applicants submit that persons skilled in the art would understand what is meant by modulators as used in the claims, and could readily discern the scope of the present invention without reference to specific modulators.

The final Office Action also states that "pages 15-17 indicate that various preclinical and clinical studies are underway to find agents that are applicable in the instant invention"and "the pages are directed to limited compounds that disclose definitive data." (final Office Action, page 3.) This is not relevant to the claimed invention. The "clinical investigations" referred to at page 16, lines 27-28 are on the use of modulators to improve drug activity by measuring plasma concentrations of drugs, not by measuring drug accumulation as set forth in the presently claimed invention. As pointed out in the disclosure, "studies directed towards clarifying uptake of [paclitaxel and docetaxel] by tumor cells would be clinically useful." (Specification, page 16, lines 30-31.) The drawbacks of possible ways of measuring drug accumulation and the advantages of the present invention are described. (Specification, page 16, line 31-page 17, line 7.) The final Office Action does not point to any data derived from clinical or preclinical studies that could or would limit the claims to specific modulators, nor any reason such limitation is necessary.

For at least the reasons set forth herein, Applicants submit that claims 8-12 (and 50-56) particularly point out and distinctly claim the invention when the content of the disclosure; the teachings of the prior art; and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made are taken into

consideration. The method of using the radiolabeled drugs in claims 8-12 and 50-56 is pointed out with particularity, and distinctly claimed and described with sufficient clarity to assure that the inventors had possession and knowledge of the claimed invention, without the need for pointing out a specific modulator. Accordingly, the rejection is clearly without basis and should be withdrawn.

Although this paper may not be the most appropriate mechanism for doing so, Applicants also traverse the withdrawal of claims 50-56 as directed to a non-elected invention. Claims 50-56 are directed to "measuring the effectiveness of modulators of cellular accumulation mechanisms in tumors . . . wherein the modulator affects tumor concentration of the anti-tumor drug or normal host cell concentration of the anti-tumor drug." Thus, the claims refer to a particular type of modulator and a search of claim 8 would encompass the subject matter of claims 50-56. If prosecution of this application proceeds, Applicants respectfully request that claims 50-56 be considered.

CONCLUSION

Applicants respectfully submit that the rejection set forth in the March 30, 2005 Office Action does not apply a correct legal standard and is therefore improper. Accordingly, Applicants submit that this application should be returned to the Examiner to issue a notice indicating the allowability of claims 8-12 and 50-56, in addition to the allowability of claims 1-7, 13-31 and 41-19.

Prompt and favorable consideration is respectfully requested.

Respectfully submitted,

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